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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,424	06/30/2003	Louis D. Falo JR.	076333-0325	8081

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,424	FALO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2005 and 07 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 2, and 4-12 are being acted upon.

2. Applicant's amendment and remarks, filed 11/07/05, and IDS, filed 8/09/05, are acknowledged. In view of Applicant's amendment, the previous rejections under 35 U.S.C. 102(b) and 103(a) have been withdrawn. Additionally, the previous double patenting rejections have also been withdrawn.

3. The declaration stands objected to because of uninitialed changes in the post office address of Inventor Falo. A new declaration is required.

Applicant indicates that a new declaration will by submitted as soon as one can be obtained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, and 4-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for, a formulation comprising a hybridoma, said hybridoma comprising a DC and a tumor cell,

does not reasonably provide enablement for, a formulation comprising a hybridoma, said hybridoma comprising a DC and a virally infected cell.

As set forth previously, A review of the specification reveals that the formulations of the instant claims are defined as "prophylactic and therapeutic agents against tumor and viral infection" (page 1), "can induce CD8+ CTL" (page 3), and "protect against viral infection" (page 4). Clearly then, the formulations of the instant claims are pharmaceutical compositions and require enablement as such. The specification provides no teachings sufficient to enable claims drawn to a DC hybridoma which induces effective anti-virally-infected cell immunity. Note that the specification discloses background references and examples that deal *exclusively* with anti-tumor DC responses and anti-tumor DC hybridomas. Anti-virally-infected cell immunity is disclosed only in concept, a concept that was not enabled in 1997.

In the case of HIV infection the situation is even more unpredictable given the fact that both DCs and T cells are infected by the virus. As taught by Frank et al. (2002):

"A dendritic cell (DC) encountering an immunodeficiency virus should pose a threat to the virus, by efficiently processing and presenting viral antigenic determinants to activate specific anti-viral T and B cell immunity. While this may

occur *in vivo*, it is apparent that DC-entrapped viruses can freely spread between cells, move to distal tissues, and proliferate rapidly particularly upon meeting CD4+ T cells. In fact, the latter is further augmented when the T cells are activated. Thus, it seems that immunodeficiency viruses exploit the unique ability of DCs to survey the periphery and capture incoming pathogens, traffic around the body often targeting the lymphoid tissues, and efficiently communicate with naive and memory T cells. Combined with the fact that DCs are likely the first leukocytes interacting with virions crossing the mucosae, these features provide the basis on which the virus maximizes its chance to establish infection even in the face of immune activation."

Given this teaching, it would seem then that the formulations of the instant claims would be more likely to exacerbate viral infections than to treat or prevent them. The reference further teaches that other viruses, including herpes simplex virus, measles virus, sendai virus, vaccinia virus, and cytomegalovirus infect DCS and down-modulate their antigen presenting functions. Accordingly, the use of the DC hybridomas of the instant claims to induce effective anti-virally-infected cell immunity would be highly unpredictable. Said unpredictability would then require undue experimentation in using the formulations of the instant claims *in vivo* as disclosed in the specification.

See also Roberts (2004, IDS); in a publication entitled, *Are HIV Vaccines Fighting Fire with Gasoline?*, the author teaches that activating T cells in an attempt to fight HIV may actually exacerbate disease. The reference notes that HIV preferentially infects, and grows better in, activated T cells (a concept known as of the priority date of the instant application). Clearly then, given the very basic questions still to be answered as recently as 2004, the formulations of the instant claims were at best highly unpredictable and requiring of undue experimentation as of the 1997 priority date.

Also note that the claims are drawn to at least one "hybridoma". As taught by Stites et al. (1987), a hybridoma comprises, "a transformed cell line grown *in vitro* that is a somatic hybrid of 2 parent cell lines". Note particularly the term "transformed". As taught be Lewin (1987) "transformed" is defined as "a state of unrestrained growth in culture, resembling or identical with the tumorigenic condition". As can be seen in Janeway et al. (1994) it is the immortal tumor cell that contributes the ability to grow indefinitely to a hybridoma. Returning to the instant invention comprising a mortal DC and a mortal virally-infected cell, it is clear that neither the mortal DC nor the mortal virally-infected cell is capable of contributing transformation/immortality to the claimed formulation, thus, in addition to failing to teach how to use the claimed formulation for its intended use (as set forth above), the specification also fails to teach how to make the "hybridoma" of the instant claims. Given the failure of the specification to teach how to make and how to use the formulation of the instant claims, said formulation is considered to be highly unpredictable and requiring of undue experimentation.

A review of the specification shows that no examples of hybridomas comprising a DC and a virally-infected cell are disclosed, i.e., no such formulations are made and none are shown to have any biological or pharmacological activity.

Accordingly, as set forth above, it is the Examiner's position that the specification fails to enable one of skill in the art to make or use the DC/virally infected cell formulations of the instant claims.

Applicant's arguments, filed 11/07/05 have been fully considered but they are not persuasive. Applicant argues that the specification teaches how to make the claimed hybridoma comprising a virally infected cell.

Applicant is advised that simply stating that the hybridoma comprises "a physical combination of at least two different cell types" and that said hybridoma can be made by "any method known in the art", including using PEG, does not comprise an enabling disclosure. For the reasons set forth previously it is unclear that a such a fusion would result in a "hybridoma", or that whatever the fusion product would comprise, that it would be effective for its intended use.

Applicant argues that the specification teaches how to use the claimed hybridoma comprising a virally infected cell and cites Maranon et al. (2004) in support. Applicant argues that the claims are directed to formulations and compositions and need not be enabled for treating all viral infections.

First note that Maranon et al. is not of record in this case and thus, need not be addressed. However, in reviewing the reference two significant points are noted. First, the publication comes some seven years after the priority date of the instant application, thus, it cannot be used to establish the enablement of the instant application as of its priority date. Second, the reference employs live antigen-loaded dendritic cells and not the fusion products of the instant claims. Also note that the reference addresses a number of issues that were clearly not known as of the priority date of the instant application, in particular, the manner in which dendritic cells take up and present antigens (note the use of the terms "unexpectedly" and "surprisingly"), a property that it is unclear whether or not the fusion products of the instant claims would possess.

Regarding Applicant's assertion that the formulations and compositions and need not be enabled for treating all viral infections, a product must be enabled for its intended use. As set forth at page 4 of the instant specification, the claimed formulations "protect against the viral infection caused by the virally infected cells used in the formulation, and/or provide therapeutic relief from patients having such viral infections". Also note that a formulation specifically comprising HIV is recited in claim 4. Further note that the compositions referred to by Applicant are actually "pharmaceutical compositions" (Claims 8-12). Clearly, the only intended use for the products of the instant claims is the treatment of viral infections, a use that is not enabled by the instant specification.

6. The following is a new ground of rejection necessitated by Applicant's amendment.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 2, and 4-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1, 2, and 4-12 of U.S. Application No. 11/089,025. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '025 application recite a formulation and pharmaceutical composition comprising a hybridoma having an antigen presenting cell fused to a virally infected cell or a tumor cell, including the limitations of Claims 2 and 4-12.

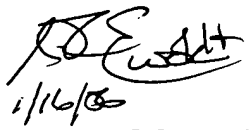
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

12. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



1/16/06

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